

**In the Specification:**

Please amend the specification as shown:

On page 13, lines 25-30:

-- Figure 32 shows aligned amino acid sequences of DSL domains from various Drosophila and mammalian Notch ligands (SEQ ID NOS 1-16, respectively, in order of appearance); Figure 33 shows amino acid sequences of human Delta-1 (SEQ ID NO: 17), Delta-3 (SEQ ID NO: 18) and Delta-4 (SEQ ID NO: 19); Figure 34 shows amino acid sequences of human Jagged-1 (SEQ ID NO: 20) and Jagged-2 (SEQ ID NO: 21); Figure 35 shows an amino acid sequence of human Notch1 (SEQ ID NO: 22); Figure 36 shows an amino acid sequence of human Notch2 (SEQ ID NO: 23); --

On page 37, line 47, to page 38, line 26:

-- A typical DSL domain may include most or all of the following consensus amino acid sequence:

Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Cys Xaa Xaa  
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa  
Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys (SEQ ID NO: 24)

Preferably the DSL domain may include most or all of the following consensus amino acid sequence:

Cys Xaa Xaa Xaa ARO ARO Xaa Xaa Xaa Cys Xaa Xaa Xaa Cys BAS NOP  
BAS ACM ACM Xaa ARO NOP ARO Xaa Xaa Cys Xaa Xaa Xaa NOP Xaa Xaa  
Xaa Cys Xaa Xaa NOP ARO Xaa NOP Xaa Xaa Cys (SEQ ID NO: 25)

wherein:

ARO is an aromatic amino acid residue, such as tyrosine, phenylalanine, tryptophan or histidine;

NOP is a non-polar amino acid residue such as glycine, alanine, proline, leucine, isoleucine or valine;

BAS is a basic amino acid residue such as arginine or lysine; and

ACM is an acid or amide amino acid residue such as aspartic acid, glutamic acid, asparagine or glutamine.

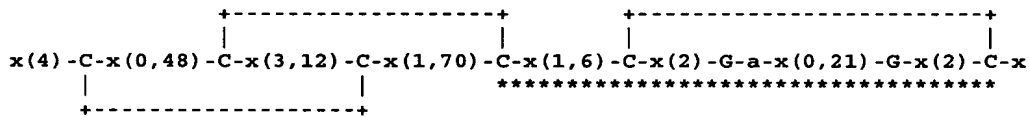
Preferably the DSL domain may include most or all of the following consensus amino acid sequence:

Cys Xaa Xaa Xaa Tyr Tyr Xaa Xaa Xaa Cys Xaa Xaa Xaa Cys Arg Pro  
Arg Asx Asp Xaa Phe Gly His Xaa Xaa Cys Xaa Xaa Xaa Gly Xaa Xaa  
Xaa Cys Xaa Xaa Gly Trp Xaa Gly Xaa Xaa Cys (SEQ ID NO: 26)

(wherein Xaa may be any amino acid and Asx is either aspartic acid or asparagine).

On page 40, lines 4-24:

-- As reported by PROSITE the EGF domain typically includes six cysteine residues which have been shown (in EGF) to be involved in disulfide bonds. The main structure is proposed, but not necessarily required, to be a two-stranded beta-sheet followed by a loop to a C-terminal short two-stranded sheet. Subdomains between the conserved cysteines strongly vary in length as shown in the following schematic representation of the EGF-like domain (SEQ ID NO: 27):



wherein:

'C': conserved cysteine involved in a disulfide bond.  
'G': often conserved glycine  
'a': often conserved aromatic amino acid  
'\*': position of both patterns.  
'x': any residue --

On page 96, line 26, to page 97, line 2:

-- Real-time quantitative PCR was performed using the Roche Lightcycler™ system (Roche, UK) and SYBR green detection chemistry according to the manufacturer's guidelines. The following HPLC-purified primer pairs were used for cDNA-specific amplification (5' to 3'):

*mouse 18s rRNA:*      **Forward** GTAACCCGTTGAACCCATT (SEQ ID NO: 28)  
                         **Reverse** CCATCCAATCGGTAGTAGCG (SEQ ID NO: 29)

*mouse Hes-1:*        **Forward** GGTGCTGATAACAGCGGAAT (SEQ ID NO: 30)  
                         **Reverse** ATTTTGGAAATCCTTCACGC (SEQ ID NO: 31) --

On page 99, lines 21-26:

-- An adenovirus major late promoter TATA-box motif with BglII and HindIII cohesive ends was generated as follows:

**BglII**

**HindIII**

GATCTGGGGGGCTATAAAAGGGGGTA (SEQ ID NO: 32)  
ACCCCCGATATTTTCCCCCATTCGA (SEQ ID NO: 33) --

On page 99, line 31, to page 100, line 4:

-- A TP1 promoter sequence (TP1; equivalent to 2 CBF1 repeats) with BamH1 and BglII cohesive ends was generated as follows:

BamH1 BglII  
5' GATCCCGACTCGTGGGAAAATGGGCGGAAGGGCACCGTGGGAAAATAGTA 3' (SEQ ID NO: 34)  
3' GGCTGAGCACCCCTTTTACCCGCCTTCCCGTGGCACCCCTTTTATCATCTAG 5'  
(SEQ ID NO: 35) --

On page 115, lines 3-8:

-- A human placental arrayed cDNA library (Origene) was screened by PCR using the following pair of primers specific for the intracellular domain of human Notch1:

hN1F: CAC CCC ATG GCT ACC TGT CAG (SEQ ID NO: 36)  
hN1R: GGC TGC ACC TGC TGG GTC TGC (SEQ ID NO: 37) --

On page 115, lines 20-29:

-- Under these conditions, the primers generate a specific diagnostic product of 500bp from a human Notch1 cDNA target. Using this PCR screening protocol, a positive human Notch1 clone (#3) was identified and sequenced to confirm its identity. Subsequently, the intracellular domain was amplified from #3 using the following primers:

hN1-IC1759: AAA GGA TTC ACC **ATG** GCA CGC AAG CGC CGG CGC AGT CAT (SEQ ID NO: 38) (contains initiation methionine in **bold**)  
hN1-IC 2556: GCG CTC GAG *TTA* CTT GAA CGC CTC CGG GAT GCG (SEQ ID NO: 39) (contains stop codon in *italics*) --

On page 116, line 10, to page 117, line 2:

-- This generated a specific product of approximately 2.6kb corresponding to the intracellular domain of human Notch1. The PCR product was digested with BamHI and XhoI (these sites are present within the amplimers) and cloned into the mammalian expression vector pcDNA3.1 (Invitrogen) using the BamHI and XhoI sites present within the multiple cloning site of this vector. The sequence of the hNotch1-IC was confirmed by sequencing, and the protein sequence encoded by this cloned sequence is as follows:

**MARKRRRQHGQLWFPEGFKVSEASKKKRREPLGEDSVGLKPLKNASDGALMDDNQNEW**  
GDEDLETKKFRFEFPVLPDLDDQTDHRQWTQQHLDAADLRMSAMAPTPPQGEVDADCM  
DVNVRGPDGFTPLMIASCSGGGLETGNSEEEEDAPAVISDFIYQGASLHNQTDRTGETALH  
LAARYSRSDAAKRLLEASADANIQDNMGRTPLHAAVSADAQGVFQILIRNRATDL DARMHD  
GTTPLILAAARLAVEGMLEDLINSHADVNAVDDLKGSALHWAAVNNVDAAVVLLKNGANKD  
MQNNREETPLFLAAREGSYETAKVLLDHFANRDITDHMDRLPRDIAQERMHHDIVRLLEDEY  
NLVRSPQLHGAPLGGTPTLSPPLCSPNGYLGSLKPGVQGKKVRKPSSKGLACGSKEAKDL  
KARRKKSQDGKGCLLDSSGMLSPVDSLES PHGYLSDVASPPLLSPFQQSPSVPLNHLPG  
MPDTHLGIGHLNVAAKPEMAALGGGGRLAFETGPPRLSHLPVASGTSTVLGSSSSGGALNF  
TVGGSTSLNGQCEWLSRLQSGMVPNQYNPLRGSVAPGPLSTQAPSLQHGMVGPLHSSLA  
ASALSQMMSYQGLPSTRLATQPHLVQTQQVQPQNLQMQQQNLQPANIQQQQSLQPPPPP  
PQPHLGVSSAASGHLGRSFLSGEPSQADVQPLGPSSLAVHTILPQESPALPTSLPSSLVPP  
VTAAQFLTPPSQHSYSSPDNTPSHQLQVPEHPFLTPSPESPDQWSSSSPHSNVSDWSE  
GVSSPPTSMQSQIARIPFAFK (SEQ ID NO: 40) --